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ERRATA

JULY 16, 1997.—Ordered to be printed

Mr. JEFFORDS, from the Committee on Labor and Human Resources, submitted the following

REPORT

together with

ADDITIONAL AND MINORITY VIEWS

[To accompany S. 830]

CORRECTIONS

On page 13, paragraph 2, line 6, after "Kennedy" insert "Harkin", line 7, transpose "Bingaman" and "Wellstone", line 17, delete "Harkin".

On page 14, paragraph 2, line 7, "delete "6" and insert "7", delete "12" and insert "11', line 14, after "Reed" insert "Mikulski", line 20, delete "Mikulski".

On page 19, line 28: Strike the word "Richard" and replace with, "William M.".

On page 63, after line 21 insert a new paragraph 9 to read:

"9. The performance goals and procedures also apply to original applications and supplements for human drugs initially marketed on an over-the-counter (OTC) basis through an NDA or switched from prescription to OTC status through an NDA or supplement."

On page 90, paragraph 1, line 1, delete "617" and replace with, "616", line 8, delete "617" and replace with "616". Paragraph 2, line 1, delete "617" and replace with "616". Paragraph 3, line 1, delete "617" and replace with "616", line 6, delete the word "fier" and insert: "date of receipt of the PMN by FDA. This section provides automatic effectiveness at the end of the 120 days unless FDA determines within that period that the notifier". Paragraph 4, line 1, delete "617" and replace with "616".

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On page 91, paragraph 1, line 1, delete "617" and replace with "616". Paragraph 2, line 1, after Section insert "(h)(5) authorizes FDA to collect". Paragraph 4, line 1, delete "617" and replace with "616", line 2, strike "establision" and insert "establishing the procedure by which FDA may deem a PMN to be no longer effective just as FDA may revoke a food additive regulation under current law. This provision". Paragraph 5, line 1, delete "617" and replace with "616".

On page 104, the additional views of Senator Wellstone were erroneously omitted, insert before the heading "ADDITIONAL VIEWS OF SENATOR MURRAY" the following:

ADDITIONAL VIEWS OF SENATOR WELLSTONE

There are many important provisions in S. 830, and I would very much like to see these provisions enated into law. While I voted in favor of the amended bill I remain concerned about a few issues that threaten to keep the bill from moving forward, and can certainly prevent me from voting in favor of the bill on the floor. The concerns that I have are related to the FDA's ability to continue to protect the public health while making the latest safe and effective therapies available to American consumers. It is my hope that responsible FDA reform that would improve the effectiveness and timeliness of the regulatory process while maintaining the safest standards that Americans count on will be signed into law this year.

While the FDA has made great strides in expediting review for certain breakthrough drugs, these efforts must be consistent across other new products and for patients suffering from all types of debilitating and life-threatening illnesses. FDA approval is recognized around the world as the "gold standard". This standard has opened markets, increased demand for U.S. products and protected consumers. But beyond looking at the FDA to protect us from unsafe products, American consumers need the FDA to do its job in a timely manner. The technologies that are regulated by the FDA change rapidly and dramatically. Americans cannot afford a regulatory system that is ill-equipped to speed those advances.

Many of the provisions in S. 830 would take a significant step toward addressing Americans' concerns with the FDA. The legislation would improve the predictability, timeliness and focus of the regulatory process for medical products. The legislation would also improve communication and collaboration between the FDA and the regulated industries. I strongly endorse the view that these objectives can be met and unnecessary regulatory burdens can be minimized without compromising the quality of the review.

COLLABORATIVE REVIEW PROCESS

Because of my interest in achieving a more collaborative process, I strongly support provisions in the legislation to encourage collaboration at the early stages of product development. The bill requires the FDA to provide applicants the opportunity to meet with the FDA officials to develop and agree in writing on a protocol for clinical studies. In addition, to facilitate collaboration and communication throughout the review process, the bill requires the FDA to

provide for a mid-review meeting, and to ensure that the applicants would be promptly notified of any deficiencies in their applications. In this way, questions could be addressed right away. I believe that improved communication and collaboration during the review process will significantly improve timeliness and benefit both patients and the regulated industries.

PREMARKET APPROVAL

I strongly endorse the committee's view that the standard proof of effectiveness for medical devices must be viewed as separate and distinct from that for new drugs. Unlike drugs, medical devices tend to evolve incrementally with new device generations often adding new therapeutic and diagnostic features. In determining the effectiveness of a device, the FDA should accept retrospective data and historical data as controls if the data are available that meet the FDA's standards for quality and completeness and the effect of the device on disease procession is well understood. This would leave the FDA the discretion it needs to conduct randomized trials when necessary while at the same time reducing costly and time-consuming requirements on applications and enabling new and innovative technologies to reach consumers in a more timely manner.

RECOGNITION OF PERFORMANCE STANDARDS TO FACILITATE MEDICAL DEVICE REVIEWS

I strongly endorse the provision that allows the FDA to recognize nationally and internationally recognized consensus performance standards and accept certification by a manufacturer that a device conforms to such standards for the purpose of facilitating medical device review. Currently, the lack of clear performance standards for the review of Class II and III devices is a barrier to the improvement of the quality, timeliness, and predictability of the review process. The FDA would retain full authority to withdraw recognition of a performance standard and to approve or disapprove a premarket application or notification.

CONSIDERATION OF LABELING CLAIMS FOR PRODUCT REVIEW

This is an extremely important provision. It is important because it more clearly states the intent of the Act with respect to the relationship of labeling claims to approval and clearance of products. For PMA's, the proposed conditions of use as indicated by the label will be the basis for determination of safety and effectiveness. This will avoid the potential for requiring that clinical outcome data, which are unrelated to device performance, safety and effectiveness, would be required for device approval. Substantial equivalence must be demonstrated for 510(k) devices, and this also would be based on intended uses proposed in the labeling of a device.

MINOR MODIFICATIONS

I strongly endorse this provision, which allows a manufacturer to make manufacturing changes to PMA (class III) products without premarket review if the manufacturer 1) submits written notice describing the change to the FDA, and 2) certifies that the change

has been made pursuant to GMP (Good Manufacturing Practices) Quality Systems Regulations. The GMP regulations currently in use incorporate requirements for pre-production design validation, which ensures that manufacturing changes may only be made if they are consistent with the design specifications of the device.

This means that any changes in the manufacturing process must be validated to demonstrate compatibility with the existing design of the device. If the original design of a device being modified has been demonstrated to be safe and effective, and a manufacturer can demonstrate that the manufacturing change does not alter the device design, then the modified device must also, by definition be safe and effective. If it is not, then it could not be considered to be compatible with the original device design. It is important to remember that the design specifications of a device involve not only the physical construction of the device, but also the actual performance of the device when it is in use. In addition, if the FDA thinks that the manufacturer does not comply with GMP's a device can be withheld from commercial distribution.

BETTER PHARMACEUTICALS FOR CHILDREN

I fully support this important provision that is designed to encourage the development of information related to the use of a drug in children. All too often, assumptions are made that children are "little adults" when it comes to the prescribing of drugs and determination of the appropriate dosage of a drug for a child. It is essential that we encourage manufacturers to explore the uses of drugs in children, and determine the safest method and dosage.

THIRD PARTY REVIEW

One of my primary concerns is the proposed structure of the pilot project for third party review of medical devices. The expansion of the pilot program to the highest risk devices is very worrisome to me and to consumers. I am not opposed to the concept of third party review, but firmly believe that any review that is conducted must meet the highest standards. As the current pilot project is barely underway, and relatively few devices have been reviewed by external reviewers, it is not time to expand the pilot program to include devices that are life supporting or life sustaining.

SUPPLEMENTAL USES OF ALREADY APPROVED DRUGS

Another provision that is troublesome is one that lowers the standard of evidence for approval of supplemental uses of drugs. In order to establish these new uses of already approved drugs, there is still a need for sound scientific evidence that a drug is effective and safe for conditions other than those for which it was originally approved. It is important that the agency allow some flexibility in the types of proof that are required for new uses, but a standard of scientific evidence should be maintained.

POST-MARKET RESEARCH REQUIREMENTS

Some drugs, which are groundbreaking therapies for serious and life-threatening illnesses, need to be made available to the public

as rapidly as possible, once it is determined that they are safe and effective, based on the use of a surrogate endpoint. Once these drugs are approved, it is important to continue to review their use and effectiveness in order to confirm their clinical benefit. At the present time, the only way that the FDA can enforce these continuing trials is to remove the drug from the market if the trials are not completed. Patients then lose access to the drug, and may suffer serious consequences. Therefore, the imposition of civil money penalties would be a useful enforcement tool in order to ensure that these studies (phase IV clinical trials) are pursued with due diligence. If structured properly, this type of provision would not place manufacturers who are making sincere efforts to continue clinical trials at risk of being penalized when the trials cannot be completed for legitimate reasons.

HEALTH CARE ECONOMIC INFORMATION

I am very concerned about this provision, as it poses a significant potential danger for consumers. As currently proposed, the provision is quite vague, and it is not clear what sort of evidence these claims could be based upon. In addition, health economics is not an exact science as individual variations and circumstances are very important when considering treatment. There is great danger in extrapolating from the whole population to a specific patient. While it is important to consider cost savings in providing treatment, there are many issues that must be taken into account when making treatment decisions. Unfortunately, we are seeing limitations in formularies in managed care plans based solely on economics. I worry that this provision will result in claims to pharmacy benefit managers that would worsen the current situation. Again, the consumer would suffer the consequences of these decisions.

I am committed to working with Senator Jeffords and my other colleagues on the committee to address these concerns and to improve some of the other provisions of the bill that may still need work, so that when the bill comes to the floor, I will be able to fully support it. The only way that we will be successful is to present a truly balanced bill that protects the public health, while providing for efficiencies to ensure that Americans have access to the safest and most effective medical products. I have a strong desire to see FDA reform legislation that has the confidence and support of the American people signed into law this year.

PAUL D. WELLSTONE.

On page 101, paragraph 4, line 3, after "indi-" insert "cation of the likelihood for industry or Congressional approval and".

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